

Claims

1. Process for obtaining chemical active ingredients
5 which are suitable for treating infectious diseases caused by unicellular or multicellular parasites, characterised in that proteins which are involved in the 1-desoxy-D-xylulose-5-phosphate metabolic pathway, or similarly acting derivatives thereof are brought into
10 contact with the active ingredients to be investigated for their activity with respect to parasites, and the active ingredients which inhibit the proteins or their derivatives are selected.

- 15 2. Process according to claim 1, characterised in that the proteins are involved in at least one of the following steps a) - i),
 - a) Converting glyceraldehyde and pyruvate to 1-desoxy-D-xylulose,
 - 20 b) Converting glyceraldehyde-3-phosphate and pyruvate to form isopentenyldiphosphate,
 - c) Forming 1-desoxy-D-xylulose-5-phosphate,
 - d) Converting glyceraldehyde-3-phosphate and pyruvate to form 1-desoxy-D-xylulose-5-phosphate,
 - 25 e) Converting 1-desoxy-D-xylulose-5-phosphate,
 - f) Forming 2-C-methyl-D-erythritol-4-phosphate,
 - g) Converting 1-desoxy-D-xylulose-5-phosphate to 2-C-methyl-D-erythritol-4-phosphate,
 - h) Converting 2-C-methyl-D-erythritol-4-phosphate,
 - 30 i) Converting 2-C-methyl-D-erythritol-4-phosphate to isopentenyldiphosphate.

3. Process according to one of claims 1 or 2, characterised in that the active ingredient inhibits the production of the enzymes involved or the co-factors involved, in particular the conversion of the enzyme 1-
5 desoxy-D-xylulose-5-phosphate-synthase or 1-desoxy-D-xylulose-5-phosphate-reductoisomerase or promotes the degradation of the enzymes involved or the co-factors involved.

10 4. Protein with or without 1-desoxy-D-xylulose-5-phosphate-synthase activity which is involved in the 1-desoxy-D-xylulose-5-phosphate metabolic pathway and a) is coded from the DNA-sequence shown in Fig. 1b and 2b or b) is coded from DNA-sequences which hybridise with
15 the DNA-sequences shown in Fig. 1b or 2b or fragments of these DNA-sequences in the DNA region which codes for the mature protein.

20 5. Protein with or without 1-desoxy-D-xylulose-5-phosphate-reductoisomerase activity, involved in the 1-desoxy-D-xylulose-5-phosphate-metabolic pathway, characterised in that it is a) coded from the DNA-sequence shown in Fig. 1a and 2a or b) coded from the DNA sequences which hybridise with the DNA-sequences
25 shown in Fig. 1a or 2a or fragments of these DNA sequences in the DNA region which codes for the mature protein.

30 6. Protein according to claims 4 or 5 and further proteins which are involved in the 1-desoxy-D-xylulose-5-phosphate metabolic pathway, characterised in that

they can be obtained from the culture supernatants of parasites or from the digested parasites by purification by chromatographic and electrophoretic techniques.

5 7. Protein according to one of claims 4 to 6, characterised in that it is a) the product of a prokaryotic or eukaryotic expression of an exogenic DNA, b) is coded from the sequences 1a, 1b, 2a or 2b or is coded from DNA-sequences which hybridise with the DNA-
10 sequences shown in Fig. 1a, 1b, 2a or 2b or fragments of these DNA-sequences in the DNA-region which codes the mature protein, or c) is coded from DNA-sequences, which would hybridise with the sequences defined in b) without degeneration of the genetic code and code for a
15 polypeptide with corresponding amino acid sequence.

8. Protein according to one of the preceding claims 4 to 7, characterised in that it consists of the amino acids of the sequences 2a, 2b, 3a or 3b.

20 9. Protein according to one of the claims 4 to 8, characterised in that the protein is 1-desoxy-D-xylulose-5-phosphate-synthase or 1-desoxy-D-xylulose-5-phosphate-reductoisomerase.

25 10. Nucleic acid, which codes a protein according to one of claims 4, to 9, characterised in that it is chosen from the group a) of the DNA-sequences shown in Fig. 1a, 1b, 2a, 2b or of the complementary DNA-
30 sequences, b) nucleic acid sequences hybridising with the sequence from a), c) nucleic acid sequences which

would hybridise with one of the sequences mentioned in
a) or b) without degeneration of the genetic code.

11. DNA, characterised in that it has a sequence
5 selected from the group consisting of the sequence shown
in Fig. 1a, the sequence shown in Fig. 1b, the sequence
shown in Fig. 2a and the sequence shown in Fig. 2b.

12. Recombinant expression vector, containing DNA,
10 which codes a protein according to claims 4 to 9 and
expresses the protein-coding DNA in a transformed micro-
organism or a transformed eukaryotic cell, or in an
animal or plant.

15 13. Host cell, in particular prokaryotic host cell,
eukaryotic host cell, animals and plants which, with a
DNA coding a protein according to claims 4 to 9, is
transfected and can produce the protein mentioned.

20 14. Host cell according to claim 13 which is E. coli or
a mammalian cell line.

15. Use of DNA which codes for a protein according to
claims 4 to 9 for the transfection of a prokaryotic or
25 eukaryotic organism.

30 16. Process according to one of claims 1 to 3,
characterised in that the protein is obtained from
parasites or culture supernatants of parasite cultures
by chromatographic and electrophoretic techniques.

17. Process according to one of claims 1 to 3 and 16, characterised in that the protein is produced recombinantly by expression of the DNA which codes a 5 protein according to one of claims 4 to 9 in a suitable host cell and isolation of the protein from the host cell or from the culture supernatant of the host cell.

18. Use of a protein from the 1-desoxy-D-xylulose-5-phosphate metabolic pathway according to one of claims 4 to 8 as antigen or immunogen for producing antibodies 10 which link this protein.

19. Antibodies against a protein from the 1-desoxy-D-xylulose-5-phosphate metabolic pathway according to one 15 of claims 4 to 9, which can be obtained by in vitro immunisation techniques or by immunising an animal with a protein according to one of the preceding claims and obtaining the antibodies from the serum or from the 20 spleen cells of the immunised animals.

20. Use of a protein according to one of claims 4 to 9 for identifying antiparasitically acting substances.

25 21. Use of an antibody according to claim 19 for identifying an antiparasitically acting substance.

22. Process for identifying nucleic acids which code a 30 protein according to one of claims 4 to 9, characterised in that the sample to be investigated is incubated with a nucleic acid probe selected from the group consisting

of a) the DNA-sequences shown in Fig. 1a and b, or the sequence complementary thereto, b) nucleic acids, hybridising with one of the sequences of a), in that the nucleic acid probe is incubated with the nucleic acid of the sample and hybridisation is optionally detected via a further binding partner of nucleic acid probe.

23. Process according to claim 23, characterised in that the nucleic acid to be detected is amplified before detection.

24. Test systems using a protein according to one of the preceding claims for identifying an antiparasitically acting substance.

25. Active ingredient for producing a pharmaceutical composition for treating infectious diseases caused by unicellular or multicellular parasites, characterised in that it is identified by using a test system according to claim 24.

26. Active ingredient for producing a herbicide or pharmaceutical composition for treating infectious diseases caused by bacteria, characterised in that it is identified by using a test system according to claim 24.

27. Active ingredient for producing a pharmaceutical composition for treating infectious diseases caused by unicellular or multicellular parasites, characterised in that it inhibits the enzymes or co-factors of the 1-desoxy-D-xylulose-5-phosphate metabolic pathway.

28. Active ingredient according to claim 25 or 27, characterised in that it inhibits at least one of the following steps a) - i),

5 a) Converting glyceraldehyde and pyruvate to 1-desoxy-D-xylulose,

 b) Converting glyceraldehyde-3-phosphate and pyruvate to form isopentenyldiphosphate,

 c) Forming 1-desoxy-D-xylulose-5-phosphate,

10 d) Converting glyceraldehyde-3-phosphate and pyruvate to form 1-desoxy-D-xylulose-5-phosphate.

 e) Converting 1-desoxy-D-xylulose-5-phosphate,

 f) Forming 2-C-methyl-D-erythritol-4-phosphate,

 g) Converting 1-desoxy-D-xylulose-5-phosphate to 2-C-methyl-D-erythritol-4-phosphate,

15 h) Converting 2-C-methyl-D-erythritol-4-phosphate,

 i) Converting 2-C-methyl-D-erythritol-4-phosphate to isopentenyldiphosphate.

20 29. Active ingredient according to claim 25, 27 or 28, characterised in that the active ingredient inhibits the production of the enzymes involved or the co-factors involved, in particular the conversion of the enzyme 1-desoxy-D-xylulose-5-phosphate-synthase or 1-desoxy-D-xylulose-5-phosphate-reductoisomerase, or promotes the degradation of the enzymes involved or the co-factors involved.

25 30. Active ingredient according to one of claims 25 to 27 characterised in that the active ingredient is 3-(N-

acetyl-N-hydroxyamino) -propylphosphonate or 3-(N-formyl-N-hydroxyamino) -propyl-phosphonate.

31. Use of an active ingredient according to claim 25,
5 27 to 30 for producing a pharmaceutical composition for
treating infectious diseases caused by unicellular or
multicellular parasites, in particular malaria, sleeping
sickness and leishmaniosis.
- 10 32. Use according to claim 31, characterised in that
the pharmaceutical composition also comprises one or a
plurality of constituents from the group consisting of
inhibitors of the fat metabolism pathways, cholesterol
synthesis or cholesterol absorption.
- 15 33. Use according to claim 32, characterised in that
the inhibitor of the fat metabolism is an HMG-CoA-
reductase inhibitor or an HMG-CoA-synthase inhibitor, in
particular Lovastatin, Mevastatin, Compactin,
20 Simvastatin, Pravastatin, Atorvastatin, Fluvastatin and
Cerivastatin.